1,188,364

PATENT SPECIFICATION

NO DRAWINGS

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International Classification:—C 07 d 33/14

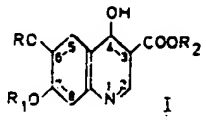
COMPLETE SPECIFICATION

Quinoline Derivatives

We, MAY & BAKER LIMITED, a British Company of Dagenham, in the County of Essex, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to new quinoline derivatives, to processes for their preparation, to compositions containing them, and to their use in the prevention of coccidiosis in chickens. It is an improvement in or modification of the invention described and claimed in the specification of our cognate copending Applications Nos. 121/67 (Serial No. 1172841) and 15666/67 (Serial No. 1146333), which is itself a modification of the invention described and claimed in the specification of our copending cognate Applications Nos. 21396/66 (Serial No. 1168801) and 35037/66 (Serial No. 1168801).

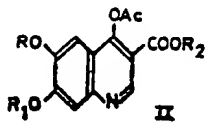
In the specification of Applications Nos. 21396/66 (Serial No. 1168801) and 35037/66 (Serial No. 1168801) we have described and claimed the 4-hydroxyquinoline derivatives of the general formula:



I

(wherein R represents a straight-chain alkyl group containing from 7 to 11 carbon atoms, R_1 represents a strait- or branched-chain alkyl group containing from 1 to 4 carbon atoms, and R_2 represents a straight- or branched-chain alkyl group containing from 1 to 3 carbon atoms) and salts thereof, which possess a very high order of anti-coccidial activity, and are useful for the prophylactic control of coccidiosis in chickens.

As a result of research and experimentation we then found that acylated derivatives of the aforesaid 4-hydroxyquinolines of the general formula:



II

(wherein Ac represents a saturated or unsaturated carboxylic acyl group, for example a group derived from a mono- or bi-cyclic aryl carboxylic acid, e.g. benzoic or naphthoic acid, an araliphatic acid in which the aryl group is mono- or bi-cyclic, e.g phenyl or naphthyl, and the aliphatic group may be branched- or straight-chain and may be an alkane group containing from 1 to 8 carbon atoms or an alkene group containing from 2 to 8 carbon atoms, a monocyclic cycloaliphatic, more especially cycloalkane, carboxylic acid containing from 4 to 9 carbon atoms, a cycloalkyl-aliphatic, more especially cycloalkyl-alkanoic, acid in which the cycloalkyl group is monocyclic and contains from 3 to 8 carbon atoms and the aliphatic chain, which may be straight or branched, contains from 1 to 8 carbon atoms, or a straight- or branched-chain aliphatic carboxylic, more

present invention for administration to chickens for the prevention of coccidiosis are solids or semi-solids in which the carrier is provided by at least part of a chicken foodstuff, i.e. an organic or mineral substance which is intended to be fed to the chickens; that is to say, the active ingredient may be incorporated in the solid or semi-solid foodstuff. Incorporation of the active ingredient in the foodstuff, which may be a commercial starter, grower, layer or breeder feed, may be effected by any conventional method such as stirring, tumbling or grinding. In this manner, by selecting different carriers and by altering the ratio of carrier to active ingredient, compositions of varying concentrations can be prepared. The active ingredient may also be incorporated in the foodstuff in the form of a powder concentrate containing it and a solid, physiologically innocuous carrier, e.g. wheat middlings, talc, kaolin or chalk or a diatomaceous earth such as kieselguhr, or a mixture thereof, and such compositions are also included within the scope of this invention. Such compositions may also contain agents to promote adhesion of the active ingredient to the carrier, for example soya oil. To the active ingredient or powders containing it, there may be added before admixture with the foodstuff, one or more physiologically innocuous wetting and/or dispersing agents, for example, the condensation product of β-naphthalene sulphonic acid and formaldehyde, sodium lauryl sulphate or polyoxyethylene (20) sorbitan monooleate. Alternatively when a wetting, suspending, emulsifying, or dispersing agent is added to the active ingredient or powder, the composition so obtained may be mixed with water to provide stable dispersions suitable for addition to foodstuffs. Compositions suitable for addition to foodstuffs which comprise the active substance in association with a wetting, suspending, dispersing or emulsifying agent, with or without a physiologically innocuous carrier, are also included within the scope of this invention. The compositions of the invention suitable for the prevention of coccidiosis in chickens, if desired, may also contain one or more additional prophylactic or therapeutic agents, for example anti-bacterial agents such as furazolidone, or coccidiostats, such as 2-chloro-4-nitrobenzamide, pyridine-3-sulphonamide, nitrofurazone or sulphaquinoxaline. Also they may contain other substances known to be useful in promoting the growth of poultry or their egg production, for example, 4-hydroxy-3-nitrophenylarsonic acid and antibiotics such as penicillin and penicillin derivatives.

Liquid compositions for oral administration may be dispersions of the active ingredient in drinking water, and these compositions may be prepared from concentrates which may be added to water, or are self-emulsifying with water. Such concentrates which comprise the active ingredient in association with one or more wetting, suspending, dispersing, emulsifying, thickening or gelling agents, with or without a physiologically innocuous carrier, or in association with a water-soluble physiologically innocuous carrier are included within the scope of this invention. Examples of these concentrates are: —

(1) Mixtures of the active ingredient with a wetting, dispersing, thickening or gelling agent, or a combination of such agents, with or without a water-soluble physiologically innocuous carrier, e.g. water;

(2) Powders comprising the active ingredient, a physiologically innocuous carrier, and a wetting, suspending or dispersing agent;

(3) Stable dispersions obtained by mixing concentrates of types (1) or (2) with water, and

(4) Mixtures of the active ingredient with a water-soluble physiologically innocuous carrier, e.g. sucrose or glucose.

Suitably dispersing agents include ethylene oxide/glyceride oil condensates, ethylene oxide/fatty alkylamine condensates and polyoxyethylene (20) sorbitan monooleate. Suitable thickening agents include sodium carboxymethylcellulose and water-soluble gums, e.g. gum tragacanth. Finely divided attapulgite clays may be used as gelling agents.

It is also possible to administer the compounds of formula III orally in the form of granules, pellets, suspensions, solutions and emulsions comprising the active ingredient in association with suitable physiologically innocuous carriers and adjuvants. Such administration is, however, generally less convenient and therefore such compositions are not preferred.

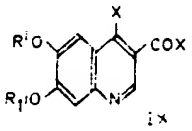
The coccidiostat compositions of the present invention may contain from about 0.0001% to about 90% by weight of one or more compounds of formula III. Concentrates for addition to chicken feed generally contain from about 1% to about 90% by weight of one or more of the compounds of formula III and preferably about 4—50% by weight adsorbed on or mixed with a carrier.

The amount of active ingredient required for effective prophylactic control of coccidiosis in chickens is very low. Good results have been obtained in the prevention of infections due to *Eimeria tenella* and *Eimeria acervulina* by the administration in feed of a quantity of active ingredient equal to about 0.0002% to 0.05% by weight of the food consumed. Optimum results are usually obtained by the daily administration of a quantity of active ingredient equal to about 0.04% to about 0.025% by weight of the food consumed.

It will be appreciated that when concentrates in the form of pellets or granules are employed as the means for administration of the quinoline derivatives, the proportion of quinoline compound present in the pellets or granules themselves is considerably higher than

IV with phosphorus oxychloride. The resultant 4-chloro compound is then hydrolysed e.g. by contacting with an acid medium, to give the required compounds of formula III, for example by boiling in acetic acid solution buffered with sodium acetate. The intermediate 4-chloro compound of formula VIII may, if desired, be separated before hydrolysis, by known methods, from the reaction mixture in which it has been prepared or, alternatively, hydrolysed without being isolated after removal of excess phosphorus oxychloride. When the symbol A in formula VIII represents a mercapto or alkylthio group, replacement of A by a hydroxyl group is preferably effected by contacting the compound of formula VIII with an acid medium, e.g. aqueous acetic acid, in the presence of an oxidising agent, e.g. hydrogen peroxide.

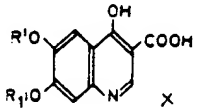
The compounds of formula VIII wherein A represents a halogen atom may also be prepared by reacting compounds of the general formula:



IX

wherein R′ and R_1 are as hereinbefore defined and X represents a halogen (preferably chlorine) atom, with alcohols of the formula R_2·OH, wherein R_2· is as hereinbefore defined.

The compounds of formula IX may be prepared from compounds of the general formula:



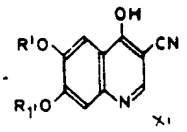
X

wherein R′ and R_1 are as hereinbefore by known methods for the conversion of hydroxy carboxylic acids into the corresponding halogeno acid halides, for example by treatment with a phosphorous halide, e.g. phosphorus oxychloride.

The compounds of formula X may be obtained

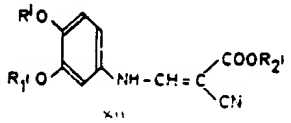
(i) by the hydrolysis of a corresponding amide or ester, e.g. a compound of formula III, for example by heating with a base such as sodium hydroxide in aqueous alcoholic solution, for example in aqueous ethanol, and recovering the acid of formula X by acidification of the solution formed, or

(ii) by the hydrolysis of a corresponding nitrile of the general formula:



XI

wherein R′ and R_1· are as hereinbefore defined, e.g. with alkali or acid by the method of C. C. Price *et al*, J. Amer. Chem. Soc., 1946, *68*, 1251. The nitriles of formula XI may be obtained by the cyclisation of an α - cyano - β-anilinoacrylate of the general formula:



XII

wherein R′, R_1 and R_2· are as hereinbefore defined. Cyclisation is preferably effected by heating the compound of formula XII at elevated temperature, for example from 180 to 350°C., and more particularly at from 200—280°C., in a suitable high boiling point solvent, for example a mineral oil, "Dowtherm" or "Diphyl".

The derivatives of formula XII may be prepared by reaction of an aniline of formula V with an alkyl orthoformate and an alkyl cyanoacetate, e.g. by the method of R. H. Baker *et al*, J. Amer. Chem. Soc., 1949, *71*, 3060, or by reaction of an aniline of formula V with an alkyl alkoxymethylene-cyanoacetate, e.g. by the method of C. C. Price, *et al*, J. Amer. Chem. Soc., 1946, *68*, 1251.

According to yet a further feature of the present invention, the quinoline derivatives of formula III are prepared by reaction of compounds of formula X with alcohols of formula R_2 OH, wherein R_2· is as hereinbefore defined. Reaction is preferably effected in the presence of a catalyst such as sulphuric acid, hydrogen chloride or boron trifluoride, the last named being conveniently used in the form of a complex with an ether such as that formed with dimethyl or diethyl ether.

According to a still further feature of the present invention, the compounds of formula III wherein R_2 represents a hydrogen atom are obtained by the transesterification by known methods of 3-position esters of compounds of formula X, for example esters wherein the hydrocarbon residue of the ester group is an alkyl group, preferably containing from 1 to 6 carbon atoms, an aralkyl group, e.g. benzyl, or an aryl group, e.g. phenyl. Preferably the 3-position ester of a compound of formula X used as starting material is another compound

aniline (0.8 g.), diethyl ethoxymethylenemalonate (0.6 g.) and ethanol (5 ml.) was heated under reflux for 15 minutes. The solvent was removed *in vacuo*, phosphorus oxychloride (2 ml.) added and the mixture heated on the steam-bath for 3 hours, then poured into aqueous sodium bicarbonate solution. The product was extracted into methylene chloride (2 × 30 ml.) and the organic extract was washed, dried and evaporated *in vacuo*. The residue, crystallised from methanol, gave ethyl 7 - allyloxy - 4 - chloro - 6 - n - decyloxyquinoline - 3 - carboxylate, m.p. 70—72°C.

The 3 - allyloxy - 4 - n - decyloxyaniline was obtained as follows:—

A solution of sodium sulphide nonahydrate (20 g.) in water (60 ml.) was added over 10 minutes to a stirred refluxing solution of 3-allyloxy - 4 - n - decyloxynitrobenzene (4.95 g.) in ethanol (200 ml.). The mixture was stirred and refluxed for 2 hours, the ethanol was removed *in vacuo*, water was added and the product was extracted into ether (3 × 250 ml.). The ethereal solution was washed and dried, and the solvent was removed *in vacuo*. The residue was dissolved in aqueous methanesulphonic acid and filtered through kieselguhr. The filtrate was basified with aqueous ammonium hydroxide and the product was extracted into ether. The ethereal solution was washed with water, dried over anhydrous magnesium sulphate and the solvent removed *in vacuo* to give 3 - allyloxy - 4 - n - decyloxyaniline as a light brown oil.

The 3 - allyloxy - 4 - n - decyloxynitrobenzene was obtained as follows:—

A mixture of 2 - n - decyloxy - 4 - nitrophenol (5.7 g.) and sodium hydride (1.0 g., a 50% suspension in oil) in dimethylformamide (50 ml.) was warmed on the steam-bath for a few minutes, then allyl bromide (2.8 ml.) was added. The reaction mixture was heated under reflux for 1 hour, poured onto ice-water (400 ml.) and the product was extracted into ether (2 × 125 ml.). The ethereal solution was washed and dried and the solvent was removed *in vacuo*. The residue, crystallised from methanol, gave 3 - allyloxy - 4-n - decyloxynitrobenzene, m.p. 36—38°C.

The 2 - n - decyloxy - 4 - nitrophenol was obtained from 4 - nitrocatechol by the method of R. F. Collins and M. Davis, J. Chem. Soc., 1961, 1863.

Example III

A mixture of 6 - n - decyloxy - 7 - ethoxy-4 - hydroxyquinoline - 3 - carboxylic acid (4.2 g.) and phosphorus oxychloride (21 ml.) was heated under reflux for 1 hour. The excess of phosphorus oxychloride was removed *in vacuo*, the residue was warmed with allyl alcohol (21 ml.) for 5 minutes on a steam-bath and the mixture was evaporated to dryness *in vacuo*. The residue was heated under reflux for 2 hours with glacial acetic acid (42 ml.) and anhydrous sodium acetate (4.2 g.), then cooled and added to ice-water (200 ml.). The product was filtered off, washed well with water, dried and crystallised from a mixture of glacial acetic acid and methanol to give allyl 6 - n-decyloxy - 7 - ethoxy - 4 - hydroxyquinoline-3 - carboxylate, m.p. 217—219°C

The 6 - n - decyloxy - 7 - ethoxy - 4-hydroxyquinoline - 3 - carboxylic acid employed as starting material was prepared as follows:—

4-Nitrocatechol mono-sodium salt (17.2 g.) was dissolved in dimethylformamide (180 ml.) and n-decyl bromide (22.1 g.) was added. The mixture was stirred and heated on a steam-bath for 1 hour and poured into water (1 litre). The precipitated solid was filtered off and dissolved in the minimum of boiling methanol. The solution was treated with sodium hydroxide solution (7.0 ml., 50% w/w) and diluted with water (500 ml.). The mixture was clarified with charcoal and filtered The filtrate was acidified with concentrated hydrochloric acid (15 ml.) and the precipitated oil extracted with diethyl ether. The extracts were washed with water, dried over anhydrous sodium sulphate and evaporated and the residue recrystallised from light petroleum (b.p. 40—60°C.) to give 1 - (2 - hydroxy - 4 - nitrophenoxy)-n - decane (11.3 g.), m.p. 46—49°C.

1 - (2 - Hydroxy - 4 - nitrophenoxy) - n-decane (10.8 g.) was dissolved in dimethylformamide (50 ml.) and the solution treated with sodium hydride (1.95 g., 50% suspension in oil). The mixture was heated on the steam-bath for 5 minutes, then treated with ethyl toluene-*p*-sulphonate (8.0 g.) dissolved in dimethylformamide (50 ml.). After heating for a further 1 hour, the mixture was poured into ice-cold water (500 ml.), made alkaline with sodium hydroxide solution, and the solid product filtered off. Crystallisation from methanol gave 1 - (2 - ethoxy - 4 - nitrophenoxy)-n - decane (10.7 g.), m.p. 50—55°C. A sample, recrystallised from methanol, melted at 53—55°C.

1 - (2 - Ethoxy - 4 - nitrophenoxy) - n-decane (10.2 g.) was reduced catalytically with hydrogen in the presence of 5% palladium on charcoal at atmospheric pressure and room temperature, and the 1 - (4 - amino - 2-ethoxyphenoxy) - n - decane obtained was converted into diethyl 4 - n - decyloxy - 3-ethoxyanilinomethylenemalonate, m.p. 38—40°C., by treatment with diethyl ethoxymethylenemalonate (6.8 g.) and cyclised in boiling "Dowtherm A" to give crude ethyl-6-n-decyloxy - 7 - ethoxy - 4 - hydroxyquinoline-3 - carboxylate (7.1 g.). A sample, recrystallised from acetic acid and methanol, melted at 244—246°C.

Ethyl 6 - n - decyloxy - 7 - ethoxy - 4-hydroxyquinoline - 3 - carboxylate (50 g.) was refluxed in ethanol (500 ml.) and water (500 ml.) containing sodium hydroxide (50 g.) for 1 hour. The solution obtained was diluted with

6 - 10′ - n - undecenyloxyquinoline - 3 - carboxylic acid, allyl 7 - ethoxy - 4 - hydroxy-6 - 10′ - n - undecenyloxyquinoline - 3-carboxylate, m.p. 202—207°C., was obtained.

The 7 - ethoxy - 4 - hydroxy - 6 - 10′-n - undecenyloxyquinoline - 3 - carboxylic acid employed as starting material was obtained as follows: —

Potassium 2 - ethoxy - 4 - nitrophenoxide (8.84 g.) was dissolved in dimethylformamide (75 ml.) and 1 - bromo - 10 - n - undecene (10.2 g.) was added. The mixture was stirred and heated on the steam bath for 1 hour, then poured into ice-cold water (500 ml.). The precipitate was filtered off, washed with water and crystallised from methanol to give 1 - (2-ethoxy - 4 - nitrophenoxy) - 10 - n - undecene (10.6 g.), m.p. 45—47°C.

1 - (2 - Ethoxy - 4 - nitrophenoxy) 10 - n-undecene (10.6 g.) in boiling glacial acetic acid (90 ml.) and water (9 ml.) was treated with reduced iron (10.6 g.) added portionwise over 2 minutes. The mixture was allowed to boil vigorously for 5 minutes before the unchanged iron was filtered off, washed with aqueous acetic acid and the filtrate diluted with water. The precipitated product was extracted into diethyl ether, the ethereal extract was washed with sodium bicarbonate solution, then with water and dried over anhydrous sodium sulphate. The solution was filtered, the solvent removed *in vacuo* to give 3 - ethoxy - 4 - 10′-n - undecenyloxyaniline as a light brown oil. This was converted into diethyl 3 - ethoxy-4 - 10′ - n - undecenyloxyanilinomethylene-malonate by treatment with diethyl ethoxy-methylenemalonate (70 ml.) and cyclised in boiling Diphyl (75 ml.). Crystallisation from dimethylformamide gave ethyl 7 - ethoxy - 4-hydroxy - 6 - 10′ - n - undecenyloxyquinoline-3 - carboxylate (7.8 g.), m.p. 232—235°C.

Ethyl 7 - ethoxy - 4 - hydroxy - 6 - 10′-n - undecenyloxyquinoline - 3 - carboxylate (5.7 g.) was refluxed in ethanol (50 ml.) and water (50 ml.) containing sodium hydroxide (7.5 g.) for 2 hours. The solution obtained was diluted with water until just turbid and filtered hot through kieselguhr. Acidification of the filtrate with concentrated hydrochloric acid gave 7 - ethoxy - 4 - hydroxy - 6 - 10′-n - undecenyloxyquinoline - 3 - carboxylic acid (5.5 g.), m.p. 250—255°C. (decomp).

According to a further aspect of the present invention, there are provided compositions suitable for administration to animals, including man, against viral infections comprising one or more of the quinoline derivatives of formula III as active ingredient in association with a physiologically innocuous carrier. By the expression "physiologically innocuous carrier" is meant a carrier which is not harmful to the animal organism. The carrier may be a solid or semi-solid or a liquid. Such compositions are conveniently produced by intimately dispersing the active ingredient through the carrier, if necessary, where the carrier is a liquid in which the active substance is but sparingly soluble, using an emulsifying, dispersing or wetting agent. In practice, the compounds of the present invention will normally be administered orally, in consequence of which the preferred compositions are those of a kind suitable for oral administration.

Solid compositions for oral administration include compressed tablets, pills, dispersible powders and granules. In such solid compositions one or more of the active compounds of general formula III is or are admixed with at least one inert diluent such as calcium carbonate, potato starch, alginic acid, or lactose. The compositions may also comprise, as is normal practice, additional substances other than inert diluents, e.g. lubricating agents, such as magnesium stearate.

Liquid compositions for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs containing inert diluents commonly used in the art, such as water and liquid paraffin. Besides inert diluents such compositions may also comprise adjuvants, such as wetting and suspending agents, and sweetening and flavouring agents.

The compositions according to the invention for oral administration also include capsules of absorbable material such as gelatin containing one or more of the active substances of general formula III with or without the addition of diluents or excipients.

Preparations according to the invention for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions or emulsions. Examples of non-aqueous solvents or suspending media are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. The compositions may also contain adjuvants such as wetting, emulsifying and dispersing agents. They may be sterilised by, for example, filtration through a bacteria-retaining filter, by incorporation in the compositions of sterilising agents, by irradiation, or by heating. They may also be manufactured in the form of sterile solid compositions, which can be mixed with steriie water or some other sterile injectable medium immediately before use.

For the treatment of domestic animals, compounds of general formula III may be incorporated in the animal foodstuff or drinking water in a manner similar to that hereinbefore described for the prevention of coccidiosis in chickens.

Compositions according to the present invention for use against viral infections may contain from about 0.002% to about 90% by weight of one or more of the compounds of formula III.

The following Example illustrates compositions according to the present invention suitable for use against viral infections.

17. Allyl 4 - cyclohexylacetoxy - 6 - n-decyloxy - 7 - ethoxyquinoline - 3 - carboxylate.

18. Allyl 4 - benzoyloxy - 6 - n - decyloxy-7 - ethoxyquinoline - 3 - carboxylate.

19. Allyl 4 - iso - butyryloxy - 6 - n - decyloxy - 7 - ethoxyquinoline - 3 - carboxylate.

20. Methyl 6 - 9′ - n - decenyloxy - 4-hydroxy - 7 - methoxyquinoline - 3 - carboxylate.

21. Process for the preparation of quinoline derivatives of the general formula specified in claim 1, or salts thereof, substantially as hereinbefore described.

22. Process for the preparation of quinoline derivatives of the general formula specified in claim 1 substantially as hereinbefore described in Example II or III.

23. Process for the preparation of quinoline derivatives of the general formula specified in claim 1 substantially as hereinbefore described in Example III, IV, V, VI or VII.

24. Quinoline derivatives of the general formula specified in claim 1, or salts thereof, when prepared by a process claimed in claim 21, 22 or 23 or by any obvious chemical equivalent thereof.

25. Compositions suitable for administration to animals which comprise at least one quinoline derivative of the general formula specified in claim 1, or salt thereof, in association with a physiologically innocuous carrier.

26. A chicken foodstuff for use in combatting coccidiosis in chickens comprising, in coccidiostatically effective amount, at least one quinoline derivative of the general formula specified in claim 1, or salt thereof.

27. A chicken foodstuff according to claim 26 in which the amount of quinoline ingredient is from 0.0001% to 0.05% by weight of the foodstuff.

28. A chicken foodstuff according to claim 26 or 27 in which the amount of quinoline ingredient is from 0.004% to 0.025% by weight of the foodstuff.

29. A chicken foodstuff according to claim 26, 27 or 28 in which the foodstuff is a chicken starter, grower, layer or breeder feed.

30. A chicken foodstuff according to any one of claims 26 to 29 in which the quinoline ingredient is the compound claimed in any of claims 9 to 20.

31. A chicken foodstuff according to claim 30 in which the quinoline ingredient is ethyl 7 - allyloxy - 6 - n - decyloxy - 4 - hydroxyquinoline - 3 - carboxylate, allyl 6 - n - decyloxy - 7 - ethoxy - 4 - hydroxyquinoline - 3-carboxylate, ethyl 7 - ethoxy - 4 - hydroxy-6 - 10′ - n - undecenyloxyquinoline - 3-carboxylate, allyl 4 - acetoxy - 6 - n - decyloxy - 7 - ethoxyquinoline - 3 - carboxylate or allyl 7 - ethoxy - 4 - hydroxy - 6 - 10′ - n-undecencyloxyquinoline - 3 - carboxylate.

32. A concentrate for addition to chicken foodstuff or drinking water comprising 1% to 90% by weight of at least one quinoline derivative of the general formula specified in claim 1, or salt thereof, in association with a physiologically innocuous carrier.

33. A concentrate according to claim 32 containing from 4% to 50% by weight of quinoline compound.

34. A concentrate for addition to chicken foodstuff or drinking water comprising at least one quinoline derivative of the general formula specified in claim 1, or salt thereof, in association with one or more wetting, suspending, dispersing, emulsifying, thickening or gelling agents, with or without a physiologically innocuous carrier.

35. A concentrate as claimed in claim 32, 33 or 34 in which the quinoline derivative is the compound claimed in any one of claims 9 to 20.

36. A concentrate as claimed in claim 32, 33 or 34 in which the quinoline ingredient is ethyl 7 - allyloxy - 6 - n - decyloxy - 4-hydroxyquinoline - 3 - carboxylate, allyl 6-n - decyloxy - 7 - ethoxy - 4 - hydroxyquinoline - 3 - carboxylate, ethyl 7 - ethoxy-4 - hydroxy - 6 - 10′ - n - undecenyloxyquinoline - 3 - carboxylate, allyl 4 - acetoxy-6 - n - decyloxy - 7 - ethoxyquinoline - 3-carboxylate or allyl 7 ethoxy - 4 - hydroxy-6 - 10′ - n - undecenyloxyquinoline - 3-carboxylate.

37. Chicken foodstuffs, or concentrates for addition to chicken foodstuffs, according to claim 26 or 32 substantially as hereinbefore described in Example I.

38. Pharmaceutical compositions which comprise, as active ingredient at least one quinoline derivative of the formula specified in claim 1, or salt thereof, in association with a pharmaceutically acceptable carrier.

39. Pharmaceutical compositions according to claim 38 substantially as hereinbefore described in Example VIII.

40. A method of preventing coccidiosis in chickens which comprises administering to the chickens a prophylactically effective amount of at least one quinoline derivative of the general formula specified in claim 1, or salt thereof.

41. A method according to claim 40 in which the said quinoline compound is administered in a chicken foodstuff containing 0.0001% to 0.05% by weight of quinoline compound.

42. A method according to claim 40 in which the said quinoline compound is administered in a chicken foodstuff containing 0.004% to 0.025% by weight of quinoline compound.